THE CURE OF GONORRHEA: AN IMMUNOLOGIC PROBLEM*

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IT was Agur, the son of Jakeh in Proverbs, who said: "There be three things too wonderful for me, yea, four which I know not," and then proceeded with his list. Now any clinician or student of medicine might easily put to shame Agur's modest list with his own ignorance, and likely high up in any such compilation would stand the way of the gonococcus in the urethra. For, despite the recent and extraordinary advancement of our knowledge with regard to gonorrhea, there still remain many factors, especially contingent upon its cure, "which are too wonderful for us, yea, which we know not."

HOW? WHY? FOR WHAT REASON?

However, the physician of today is no longer content to accept the cure of gonorrhea as the inscrutable mystery of the past, but seeks rather to ascertain the how? why? for what reason? of it all. For upon the correct answer to these questions hinges the genesis of more efficient therapy with its intelligent application. This quest for the proper answer is somewhat simplified by the tabulation of certain basic concepts at the outset:

1. An attack of gonorrhea represents a protean struggle between two hostile and oppugnant forces. On one side a living organism—the gonococcus—seeks establishment in the urethral tissue and, if successful, will be manifested by local tissue damage or necrosis. On the other the body's defense mechanism attempts to localize the invasion after initial fixation has occurred, which is manifested by inflammation contingent upon the local tissue injury.

2. Tissue damage—the epitasis of this drama—is essential to the biologic welfare of the gonococcus, since it supplies nutritional prerequisites. It is also beneficial to the body, since it leads to mobilization of the defense mosaic.

3. This struggle is conditioned in a general way by the virility of the organism (*i. e.*, the degree of tissue damage), the susceptibility of the tissue involved (*i. e.*, tissue anatomy), and the efficacy of the body's defense mechanism (*i. e.*, inflammation and healing).

4. Apparently when the defense mechanism is triumphant (*i. e.*, when complete tissue immunity accrues) the disease is cured.

5. The defense mosaic is amplified and the advent of complete immunity speeded by adroitly undermining the invader's fortunes.

After all, the physician who intelligently treats gonorrhea merely crusades in behalf of the defense mechanism, strives to limit the invader's depredation, and thus hastens the development of complete tissue immunity. His therapy may bring biologic adversity to the gonococcus (induced fever or chemotherapy—currently sulphanilamide), or seek primarily to fortify the defense mosaic in judicious use of the filtrate; but, in any event, all rational therapy must be conditioned by some understanding of this struggle, and hence some knowledge as to the biology of the gonococcus and the body's defense mechanism. These factors will be attempted in logical sequence.

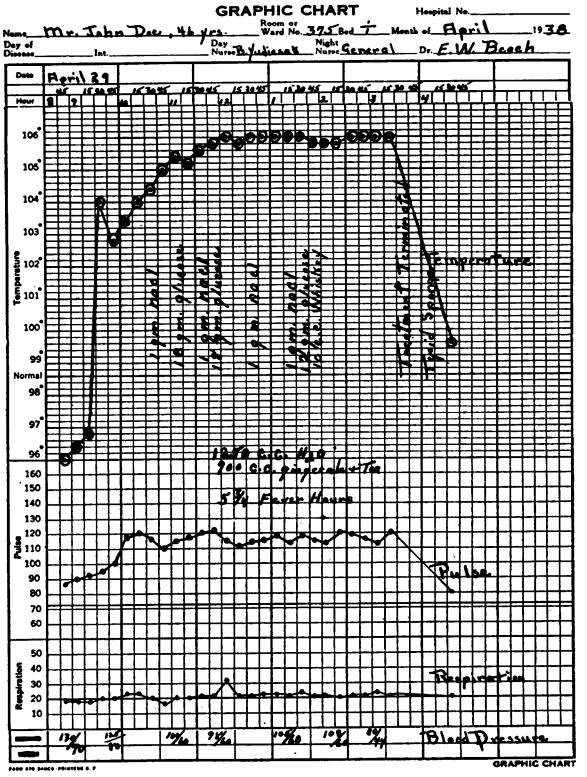

Fig. 1.—A typical hyperpyrexia chart. All temperatures taken per rectum at fifteen-minute intervals and in consonance with pulse and blood pressure determinations. Note steadfastness of temperature elevation. Note pulse rate in relation to temperature.

BIOCLINICAL ASPECTS OF THE GONOCOCCUS

This microörganism, like other bacteria, is a unicellular bit of living protoplasm—the cytoplasm being known as the endoplasm, the cell membrane the ectoplasm. The existence of nuclear material in the endoplasm is debatable. All bacteria as living organisms have the usual biotic potential and all reproduce by fission. Bacteria are the oldest known of living things—with ancestral lineage likely in the pre-Cambrian era. Originally, all bacteria were scavengers or saprophytic by nature, and functioned to destroy dead animal and plant residue. While it is questionable, in a phylogenetic sense, whether all bacteria had common origin, yet in the process of mankind's evolution certain bacteria began to attack living tissue, *i. e.*, they became pathogenic. Thus began an eternal struggle between the unicellular invader, or pathogen, and the complex defense mechanism of the body, so that each individual body cell thereby acquired, physiologically, a relative degree of immunity. Moreover, certain pathogens have become so highly selective

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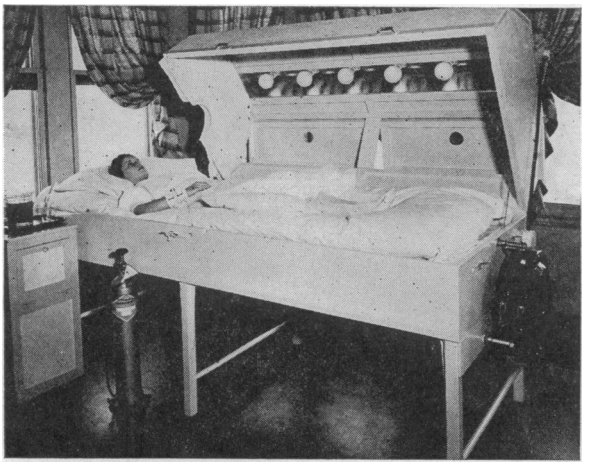

Fig. 2.—Cabinet opened. Patient rests upon feather tick over mattress. Note the five 250-watt CX Mazda bulbs in compartment above protected by wire mesh. Note Cutler-Hammer rheostat at end of cabinet to regulate current to lights.

in their biologic demands that life and growth are possible only in certain tissues of the body, and only under certain physiological conditions. Such an organism is the gonococcus, which has become a strict parasite by reason of its close association with mankind from time immemorial. Moreover, for the same reason a condition approaching symbiosis has evolved. In other words, so dependent has the gonococcus become upon the host for its complex and preformed growth requirements that it has entirely lost the necessary power to synthesize its own from more elemental pabulum. As a heterotrophic organism, therefore, life outside the body is quite impossible save on "enriched" media (blood or tissue juices added) and under most exacting conditions. Only the viruses, which will not grow at all upon artificial media, are more fastidious as to biologic requirements than the gonococcus.

The highly selective nature of this parasite—the gonococcus—is affirmed by its preference for columnar epithelium and transitional epithelium with a physiologically nondistensible and closely attached subjacent strata. Moreover, constant association with the isothermic host has established the optimum temperature for this organism at or near 98.6 degrees Fahrenheit. Clinical observations in the course of intercurrent febrile maladies have long attested its thermolabile nature. It is cultured with difficulty from febrile patients, according to Neisser and Scholtz.[1] It will not grow on culture media at temperatures above 100.4 degrees Fahrenheit.

It would appear, therefore, that the gonococcus is quite vulnerable from the standpoint of heat or induced fever (remembering fever as the body's universal response to infection) and especially since a condition of near symbiosis has been established so that this infection is almost afebrile or attended usually by a minimum of temperature elevation. Much scientific work by Carpenter, Boak, Mucci, Warren[2] and others has been done to determine accurately the thermal death point of different strains of the gonococcus *in vitro*. About 99 per cent are destroyed at 105.8 degrees Fahrenheit within four to five hours. Although conditions *in vitro* and *in vivo* are by no means consonant, this point in many instances may be safely exceeded without injury to the body with nicely controlled artificial fever apparatus. Lower ranges of fever for briefer periods of time apparently attenuate the organism or inhibit its growth in the tissues.

Incidental to countless sorties upon the favorable soil of the host, the gonococcus has developed a protective mechanism of its own. Exact knowledge anent the toxin, elaborated by the gonococcus, poses the profession as yet. It has long been thought to be an endotoxin, *i. e.,* an insoluble principle tightly bound to the protoplasm of the organism. If this be true, then the antibody contribution to the chain of immunologic events is overshadowed by local tissue developments and phagocytic activity. On the other hand, Ferry's work[3] on both the gonococcus and meningococcus indicates the presence of a soluble principle, *i. e.,* an extracellular toxin capable of sponsoring antitoxin production.

Sulfanilamide.—Sulphanilamide—a forerunner in that intricate and as yet little-understood field of chemotherapy—has established clinical value against the hemolytic streptococcus,[4] the meningococcus,[5] and the gonococcus.[6] Since these organisms have much in common (family Coccaceae) and all have exotoxins, it seems logical to assume identical *modus operandi* for the drug in each instance. Recent investigation of the action of sulphanilamid by Osgood and Brownlee[7] (limited to beta hemolytic streptococcus) indicated that this drug neither promoted phagocytosis *per se* nor assailed the organism directly, but behaved rather as an antitoxin to neutralize the toxin.

The efficacy of sulphanilamide in gonorrhea apparently depends upon (1) the proper concentration (above 1-100,000) of the free form (para-amino-benzene-sulfonamid) in the body fluids, and (2) its continuous maintenance for lengthy periods so as to completely disarm the gonococcus and thus prevent tissue damage. For without tissue damage the parasite's nutritional demands cannot be satisfied, and hence the life cycle is interrupted. Clinical fulfillment of the above postulates is arduous because the metabolic endpoint for sulphanilamid varies preponderantly with the individual—an admixture of the free form, which is useful, and the acetyl form, which is both inert therapeutically and somatically toxic in quantities—and because of the rapid elimination rate for the drug (three- to four-hour interval). Haphazard administration of sulphanilamid is, therefore, under the circumstances, not only fatuous but positively dangerous, since any drug (and particularly with the benzene ring) operating in that narrow and shadowy zone between the living protoplasm of the body cells and the living bacterial protoplasm (with supposedly low toxicity for the former, but selective affinity for the latter or its vital process) is liable to vitiation, specific deviation or even reverse application under modified or unusual physiologic conditions. Hence, vigilance anent sulphanilamide is necessary, pending more comprehensive pharmacological knowledge.

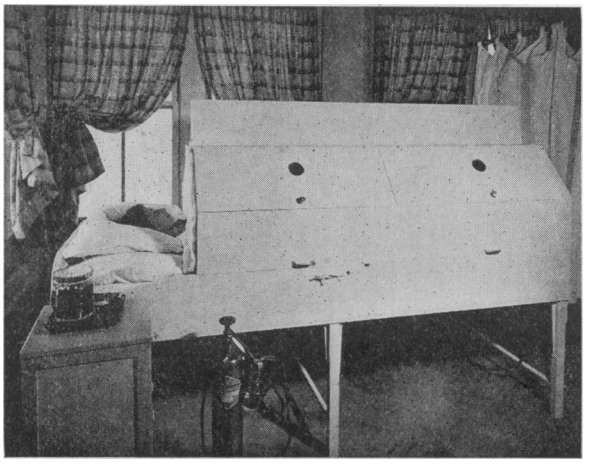

Fig. 3.—Homemade celotex cabinet molded after the original ideas of S. L. Warren. Note glass apertures for view of interior. Note terry cloth drapery about neck to seal interior. Note large panels to facilitate opening and care of patient.

THE DEFENSE MECHANISM

There are presently three interrelated and complementary parts to the mosaic of the defense mechanism, to wit: (1) the humoral attribute, *i. e.*, the antibodies; (2) the cellular attribute, *i. e.*, the fixed and mobile phagocytes; and (3) the local tissue attribute. Clinically, the rôle of local tissue immunity (3) is the most important in gonorrhea, yet, unfortunately, it is the least understood of all these attributes. Knowledge anent (1) and (2) is now fairly extensive, but its completion also must await better understanding of (3). Certain concepts, as outlined by R. Kahn[8] in his book on "Tissue Immunity," are followed herein.

The Incubation Period.—Although the columnar epithelium is most susceptible to the gonococcus, a relative degree of immunity must exist else no fixation of the organism nor its antigen could occur, and hence no tissue damage would result. The incubation period represents the time required for anchoring of the organism and hence for tissue damage to accrue.

Subsequent Possibilities.—With the advent of tissue damage (which, physiologically, is the exact opposite of inflammation), all defense attributes are stimulated, and particularly (1) and (2), so that an inflammatory bulwark (comprising accumulated fluids, phagocytes, bacteriolytic, and proteolytic substances) is interposed between the invader and the deeper tissues to prevent extension of the process. Great virulence of the organism—slow tissue response or temporary tissue disimmunity—may permit the gonococcus to enter the deeper tissues and the blood stream. The struggle now goes forward with either the host or parasite currently triumphant from time to time in this preformed inflammatory box. Destruction of the organism may occur rapidly and particularly if the organism can be locked tightly in the tissues. If the organism continues in ascendancy with the production of more tissue necrosis, an abscess results with evacuation of the contents and often into the urethra. Since every shade of tempo is possible, the organisms may continue viable for lengthy periods within these inflammatory ramifications, causing little or no destruction of tissue. Eventually healing is consummated with restoration of function, either partial or complete.

In due course when all the tissues (local—antibodies and phagocytes) have developed selective affinity for the antigen, complete immunity is established. Undoubtedly, the specific adaptation of the tissues, fluids, and phagocytes alike to the antigen is fundamentally of the same general nature although entirely dissimilar as to manifestations.

THE STRUGGLE

The intimate details of this struggle, which are presently more philosophical than factual, constitute no ensemble. Only fragmentary data from several sources are available, and yet some correlation must be attempted despite existent hiatuses. Knowledge of colloidal phenomena, p^H values and biocatalysts is helpful. New horizons prevail anent substrates, growth factor prerequisites, oxidation-reduction potentials, bacterial chemosynthesis, respiration, and metabolism generally.[9] Yet these but accentuate the absence of other essential pieces to this jigsaw puzzle.

The antigen elaborated by the gonococcus is by nature a lyophilic colloid and when combined through adsorption with the tissues causes destruction of the latter. By the secretion of exo-cellular enzymes the gonococcus reduces this complex, broken-down tissue to simpler and more diffusible combinations. In turn, this more diffusible product is acted upon by endo-enzymes and assimilated by the organism to supply energy in its life cycle. That accumulated catabolic end-products or "respiration" by-products act as "pressor" substances to inhibit the growth of the organism seems plausible and in accord with the biologic behavior of other microörganisms. Likely this explains the clinical observation that structures with poor but intermittent drainage are so adamant to treatment.

The mechanism for antibody production in response to the antigen is vague at present. Whether the antibodies are new substances entirely or modified globulin fractions of the normal blood serum with the antigen "imprint" awaits discovery. Their specificity likely has to do with stereochemical spacing or formation of a template on the newly arranged protein.

CLINICAL APPLICATION

All expedients entering into the candelabrum of intelligent therapy have common objectivity and are theoretically complementary. These may be divided arbitrarily into (1) expedients which primarily amplify the defense mechanism; (2) expedients which primarily assail the parasite; and (3) expedients primarily equipollent and which operate simultaneously.

Supplementation of the Defense Mosaic.—The clinician comes to realize that while cure may depend upon the body's mechanism for parenteral digestion or destruction of the gonococcus and its antigenic agent, this is essentially a slow-moving, time-consuming and delicately balanced process. Moreover, while it is efficient when the offender is

a prisoner (incarcerated in the tissues) or when the organism has complete freedom (good drainage), it is often inadequate or uncertain when the parasite is on parole (intermittent drainage) or when complications arise. Since, in light of our present knowledge this defense mechanism lacks completeness, the clinician is often reluctant to undertake direct augmentation lest he inadvertently champion the parasite's fortunes at the expense of the host. For this reason, and despite theoretical advantages, the practical physician usually avoids injections of specific or nonspecific proteins or the intradermal use of the filtrate "antivirus" or other antigen-like substances in gonorrhea. The filtrate especially is a two-edged sword and as such has potentialities for harm—chiefly immunologic "fatigue" and disimmunity production.

Direct Attack Upon the Gonococcus.—Manifestly, once tissue damage develops and the organism is established, it is questionable whether any local injection can even contact the parasite, let alone destroy the latter. The clinical value of irrigations is likely contingent upon better drainage. Tissue damage is a biologic necessity for the gonococcus since, as a specialist, it has replaced plebeian tastes with a capricious appetite; hence any expedient which precludes or minimizes tissue damage is most valuable. It is, therefore, beholden upon the physician to prevent tissue damage (hence the strategy of acriflavin attack in the incubation period) or to limit the degree (hence to avoid strong injections, trauma, alcohol, coitus, etc.) once it accrues. Sulphanilamide appears especially apt in this respect, since if the toxin is neutralized, tissue destruction is impossible.

An Equipotential Modality.—The fever syndrome depends upon extraordinary acceleration of vital body activity, and the greater the physiologic exaltation the higher the temperature. The theory of induced fever is predicated upon the corollary: the higher the induced temperature or "forced draft" (within certain limits) the greater the enhancement of physiologic activity. Since each body cell has inherently a relative quota of physiologic immunity, it appears that the latter should, therefore, be augmented and somewhat in proportion to the degree of hyperthermia. Induced fever seems to stimulate the defense mechanism[10] in gonorrhea and also to assail the gonococcus simultaneously. We have proved the clinical value of induced fever as a supplement to other forms of therapy in the treatment of gonorrhea over a long period. Our objective with this modality has been to strengthen or fortify certain weak or inadequate links in the chain of immunologic events leading to the goal of complete tissue immunity, and also to sponsor a biologic environment inimical to the parasite's welfare. Accordingly we have focused our attention upon the patient and his tolerance—not the organism and its precise lethal point. If well tolerated, we endeavor, for four to five hours, to maintain the temperature steadfastly at 105.5 to 106 degrees Fahrenheit, taken rectally at ten-minute intervals and in consonance with pulse and blood pressure determination. In this way and by repetition if necessary, we have obtained gratifying results with a minimum of danger. Induced fever appears most useful in complicated phases of the disease, particularly so-called gonorrheal arthritis and with resistant strains of the organism. After much preliminary experimentation with high-mettled machines for short-wave production, we now use a simple inexpensive home-made celotex cabinet, modeled after the original ideas of Stafford Warren[11] and equipped with five 250 watt CX Mazda bulbs for direct radiation. This is both practical and controllable.

IN CONCLUSION

1. About a century ago Philippe Ricord, with his famous *bon mot,* "We know when clap begins, but God alone knows when it ends," apparently crystallized the truth in that the cure of gonorrhea is always contingent upon and incident to complete tissue immunity.

2. Since our knowledge of this mechanism—which involves alike the antibodies, phagocytes, and local tissues—is still incomplete, the rationale of attack as to the biology of the gonococcus, which is better understood and which complements the defense forces, is apparent.

3. The two innovative expedients for this purpose (currently sulphanilamide and induced fever) while not exactly comparable apparently operate in much the same manner. Of the two, induced fever is the more certain and, if intelligently used, more closely approaches the ideal form of therapy.

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DISCUSSION

ARNO G. FOLTE, M.D. (1063 Flood Building, San Francisco).—Doctor Beach has just presented to us a very complete study of the immunologic aspects involved in the treatment and cure of gonorrhea. The vital question that comes to my mind is how we are going to profit from an understanding of these principles, which should make us into better clinicians. Most of these immunologic precepts are not new, and hold true in the treatment of any acute, pyogenic infection. It has often been repeated that gonorrhea is a self-limited disease, but this expression implies that we should attack gonorrhea by maintaining a strictly hands-off policy, and allow the defensive mechanism to operate and cure the patient. Perhaps this is what happens in the end; but none of us feel so impotent that we don't believe we can assist in this immunologic process in a helpful way. We know by experience that tissue immunity is a sensitive process, to be hindered, or enhanced, during treatment, according to the ability of the physician.

But whatever method of treatment we pursue it must be with an understanding of the three fundamentals which Doctor Beach has stressed, *i. e.*, first, a knowledge of the biologic life of the gonococcus; and, secondly, tissue defense mechanism. By tissue defense mechanism, we mean that a cure depends mainly on local tissue immunity, aided perhaps by the development of humoral antibodies, if Ferry's work on the exotoxin of the gonococcus is substantiated. Thirdly, tissue anatomy. This latter, because the gonococcus is a selective organism, and solely concerned with columnar-cell surfaces, such as are found in the anterior urethra and glands connected to it, and those transitional cell surfaces that are firmly attached to their subadjacent structures, as in the posterior urethra and trigone.

Inasmuch as tissue immunity is a variable quality in different patients, and not predictable in regard to the time element, and since most of our attempts to speed it up have frequently ended disastrously to the patient, it is encouraging to note that with recent advances in chemotherapy and fever therapy, a step forward seems accomplished.

I might add, that whatever method of treatment we follow, be it with injections, irrigations, filtrates, foreign proteins, fever, and the like, these must be used by keeping ever in mind the immunologic picture of the disease. Local tissue immunity is sometimes fleeting and cannot be measured by any sort of gauge or meter; but by careful and frequent observation much of this process can be estimated, and, with experience on the part of the physician, be aided.

I fully agree with Doctor Beach's conclusions that, with the advent of sulfanilamide and induced fever therapy, we approach a more rational attack on the disease, and the modus operandi of which fits in well with our ideas of the defense mechanism of the human host.

JOHN G. CHEETHAM, M.D. (538 Medical Arts Building, Portland, Oregon).—The essence of Doctor Beach's paper is to the effect that cure of gonorrhea is always contingent upon and incident to complete tissue immunity. The outlined defense mechanism which contributes toward this end is concerned, separately and in combination, with antibodies, phagocytes, fixed and mobile; and with local tissue attributes.

Therapeusis is concerned with those expedients, as vaccine, which amplify the defense mechanism; with those expedients as local therapy and sulfanilamide which may primarily assail the parasite; and with those expedients as fever therapy which in dual manner contribute both to immunologic defense and have direct action on the invading organisms.

Let us consider briefly the four principal agencies in the treatment of gonorrhea. By the use of local therapy we endeavor to accomplish adequate drainage, to build up a certain degree of local immunity, and to achieve a certain amount of germicidal action. The advent of newer remedies should not allow us to forget and discard this method of treatment which in the past has fulfilled the therapeutic requirements of a multitude of cases and which, when used in conjunction with these newer remedies, gives greater effectiveness than can be acquired by the use of such agencies alone.

With regard to the second agency, we agree that the immunological balance in gonorrhea is so delicate that, while vaccines and filtrates may be theoretically of advantage, yet both qualitative and quantitative factors in dosage and response are so variable that immunity defenses may be overthrown rather than built up. We do not ordinarily employ their use.

The third agency, artificial fever therapy, exhibits a definite thermolabile effect, but its preponderant activity lies in the formation and mobilization of immune bodies. The leukocytoses developed plays an important part in phagocytosis. In cases resistant to other medication, and in those patients who can tolerate it, hyperpyrexia is a valuable aid in the treatment of gonorrhea.

The last agent, sulfanilamide, has a bacteriostatic and bacteriolytic effect of a nature different from but supplementary to hyperpyrexia. Its chief effect is probably in the neutralization of bacterial toxins, thereby allowing the bactericidal properties of the blood serum and of the phagocytes greater activity. Used alone, while of immense value, this drug has not furnished the remarkable results that early reports in the literature indicated for it.

Since the attributes of these agencies vary in kind and degree, it would seem logical that a combination of two or more would be more effective than any one alone.

Superior results are being obtained with the use of local therapy and sulfanilamide combined—probably 75 per cent of cures within a time limit of six weeks.

Even more successful are the results from the dual use of sulfanilamid and artificial fever therapy. It is worthy of note that with this method the dose of the drug need not be so large nor the fever maintained at so high a level as when those modalities are used alone. When to this combination we add local therapy we feel that we have amassed together all of the essential elements in the treatment of gonorrhea; and therapy with this triphasic method is at the optimum. This triphasic treatment is not recommended as a routine, but is indicated for those cases which have failed of cure by other methods and for those patients in whom a quick and experient cure is necessary.

Of less import than the fact that by this method we have been able to secure 90 per cent cures within a period of two weeks' time—is the evidence that definite studies along the lines of immunity—such as today presented by Doctor Beach—are going on and from these the knowledge may come whereby, if we cannot hope for complete eradication of this disease, yet we may anticipate an early improvement in its control.

JAY J. CRANE, M.D. (1921 Wilshire Boulevard, Los Angeles).—Doctor Beach's timely paper was received with favorable comments at the time it was given before the Section on Urology. His comprehensive explanation of the rational theories pertaining to the ultimate cure of gonorrhea were very enlightening. No statements were made relative to certain drugs or methods which had not been well tried in Doctor Beach's private practice, and his conclusions were based upon carefully made observations with a full knowledge of what others had been doing and what they thought.

Sulfanilamide, more than fever therapy, has given to the practitioner an effective drug which, in a large measure, can be considered as a specific against gonorrhea, thereby greatly shortening the course of the disease in many patients.

I am very glad that Doctor Beach's paper is published in a journal read largely by general practitioners, so that they may have a more clear understanding as to what part this drug plays in helping to eradicate this disease. Many think of sulfanilamide as a sterilizing agent, but it undoubtedly is not, as Doctor Beach has pointed out. One is apt to believe also, from the extensive use of the drug, that it is not very toxic. This thought is also wrong, for there is practically no one that takes the drug that is

entirely free of toxic symptoms. Nevertheless, its discovery has been a great step forward in the treatment of gonorrhea and its use should be cautiously continued.

Fever therapy, more difficult of administration than sulfanilamide, is undoubtedly very useful, but it has never become popular with the general practitioner because of the equipment required, and the supervision necessary in carrying out treatments. I believe that had sulfanilamid not been discovered when it was, fever therapy would be used more extensively today. Of the two methods, I believe the prescribing of sulfanilamide is less dangerous and accomplishes more.

The determination of cure is still difficult and should be carefully checked, as in the past, by all of our old methods, *i. e.*, prostatic massages, sounds, smears, and close observation over a period of several months, after a complete absence of all symptoms.

HERPES ZOSTER: TREATMENT WITH THIAMIN CHLORID

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DISCUSSION *by J. F. Walsh, M.D., Eureka; Orris R. Myers, M.D., Eureka; Arne Ely Ingels, M.D., San Francisco.*

THE pathology of herpes zoster is essentially an inflammation of the posterior root ganglia, causing a degeneration of some of the posterior root and of the peripheral nerve fibers. The skin lesions are erythematous patches, which soon change to vesicles and are found along the distribution of the affected nerve or nerves.

The initial symptom of this disease and one which, along with the dermatosis, presents the most prominent feature, is pain. This is, of course, due to the inflammatory process in the posterior root, but may also be attributed to the degenerative process occurring in the peripheral nerve tract. It may be likened to the pain in thrombo-angiitis obliterans, which is due to the nerve degeneration accompanying the circulatory disturbance (ischemic neuritis). In this latter condition it is a common belief that the pain persists until the process of nerve degeneration has been completed.

Herpes zoster may be divided into two etiologic types: (1) The symptomatic, which may be due to syphilis, spinal-cord tumor, vertebral disease, and arsenic poisoning, and (2) the essential type, which may come in epidemics, and is probably due to a virus. The treatment in the symptomatic type is obvious if, and when, the diagnosis is made. However, in the essential type, the chief treatment has consisted of alleviation of pain with salicylates, and the local care of the lesions. We have used pituitrin with questionable results.

Since the beneficial influence of vitamin B_1 or thiamin chlorid in neuritis, and its prevention of certain degenerative nerve changes is acknowledged; and since it has been established that the prominent feature in herpes zoster is a neuritis with degenerative changes, we had occasion to treat five such cases with subcutaneous administration of thiamin chlorid with gratifying results. These are herewith submitted:

REPORT OF CASES

CASE 1.—G. W., male, age 49. Occupation, woodsman. Appeared on October 27, 1938, complaining of severe pain in right hip and right chest of about five days' duration. Two days prior, there appeared a rash on the right side of his chest. Past history included an injury to his lumbar region in April, 1937, when he fell a distance of twelve feet. There were no fractures at that time, but a period of five months was required before he was released from treatment. Since then he has enjoyed good health. Examination at this time was essentially negative, except for herpes zoster along the course of the twelfth dorsal nerve. Wassermann was negative. At this first visit the patient was treated by cleansing the lesions[1], and sodium salicylate was prescribed. He returned on October 31, 1938, complaining that the pain was only slightly relieved by salicylates. At this time he was given thiamin chlorid, 3000 units, hypodermically, and again on November 1, 1938. He returned on November 3, 1938, stating that for the first since the onset of his condition he had had a good night's sleep, and that at present he was entirely free from pain. He was again given a 3000-unit dose of thiamin chlorid, and this was repeated on November 5, 1938. At this last visit his lesions showed definite signs of healing and he was entirely free from pain.

* * *

CASE 2.—R. G., age 48, millwright. Admitted on November 17, 1938, complaining of a rash on left side of his chest, with severe pain in that area. The rash had appeared the day before. His condition was a herpes zoster along distribution of the eighth dorsal nerve on the left. Wassermann was negative. Examination otherwise was essentially negative. He was treated with thiamin chlorid, 3000 units hypodermically, on November 17, 18, 19, 21, 22, and 23. His pain had disappeared on the 19th, after two doses, and he was discharged from treatment with the lesions almost completely healed on November 23, 1938.

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CASE 3.—G. S., male, age 22, mill worker. Came in on November 23, 1938, complaining of a rash in the right chest area, of three days' duration. Since the onset, there was a slight pain in his back with severe burning in the herpetic lesions. Examination was essentially negative, except for herpes zoster—distribution along the tenth and eleventh dorsal nerves on the right. Wassermann was negative. He was given vitamin B_1 3000 units by hypodermic, on the following dates: November 23, 25, 26, 28, 30, and on December 2 and 5. The pain was improved slightly on November 26, and had entirely disappeared on November 28. The lesions showed some healing on November 30, and were completely healed on December 7, at which time the patient was discharged from treatment.

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CASE 4.—I. W., female, age 15, student, appeared in the clinic on December 20, 1938, complaining of "shooting" pains in the left shoulder for the past six days. The pain was aggravated by motion. On December 17, 1938, she began to have itching on the shoulder and on the left arm. On December 19 she noticed a rash on the inner aspect of the arm, on the left breast, and over the left scapula. There was some pain in the left wrist. Examination revealed herpes zoster of the areas mentioned. She was given thiamin chlorid, 3000 units hypodermically, on the following dates: December 20, 21, 22, 23, 24, and 27. Progress was as follows: There was marked improvement from pain on December 22, and she was able to move her shoulder without discomfort. There were no additional lesions present. On December 23 she complained of having had a few spasms of mild pain in the shoulder early in the morning, but when seen at the office these had entirely cleared. On December 24 she felt practically normal again, and the lesions were drying. At the last visit, on December 27, the patient was apparently cured. The lesions were gone, except for small, dry, erythematous patches in their place.

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CASE 5.—C. V. J., male, age 71, retired, appeared on December 17, 1938, complaining of pain in the right chest for the past two weeks. For two days prior to admission he had noticed an erythematous rash on the right chest, extending along the distribution of the fifth and sixth dorsal

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[1] Note: The lesions in all five cases were painted daily with tincture of merthiolate in collodion.